

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization  
International Bureau



(43) International Publication Date  
27 September 2001 (27.09.2001)

PCT

(10) International Publication Number  
**WO 01/70757 A3**

(51) International Patent Classification<sup>7</sup>: C07C 323/20,  
323/60, C07H 15/203, A61K 31/70, A61P 29/00, 3/06

(21) International Application Number: PCT/US01/09049

(22) International Filing Date: 21 March 2001 (21.03.2001)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:  
60/191,046 21 March 2000 (21.03.2000) US

(71) Applicant (for all designated States except US):  
ATHEROGENICS, INC. [US/US]: 8995 Westside  
Parkway, Alpharetta, GA 30004 (US).

(72) Inventors; and

(75) Inventors/Applicants (for US only): MENG, Charles, Q.  
[CA/US]: 725 Northerden Court, Alpharetta, GA 30005  
(US). HOONG, Lee, K. [MY/US]: 220 Gaines Oak  
Way, Suwanee, GA 30024 (US). SOMERS, Patricia, K.  
[US/US]: 201 Yale Way, Fort Collins, CO 80525 (US).

(74) Agent: KNOWLES, Sherry, M.: King & Spalding, 191  
Peachtree Street, Atlanta, GA 30303-1763 (US).

(81) Designated States (national): AE, AG, AL, AM, AT, AU,  
AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU,  
CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM,  
HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK,  
LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX,  
MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL,  
TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.

(84) Designated States (regional): ARIPO patent (GH, GM,  
KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian  
patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European  
patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE,  
IT, LU, MC, NL, PT, SE, TR), OAPI patent (BF, BJ, CF,  
CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).

Published:  
--- with international search report

(88) Date of publication of the international search report:  
14 March 2002

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 01/70757 A3

(54) Title: THIOKETALS AND THIOETHERS FOR INHIBITING THE EXPRESSION OF VCAM-1

(57) Abstract: Thioketals and thioethers are provided that inhibit the expression of VCAM-1, and which can be used in the treatment of VCAM-1 mediated diseases including inflammatory disorders, cardiovascular diseases, ocular diseases, autoimmune diseases, neurological disorders, and cancer. The compounds also can be used to treat hyperlipidemia and/or hypercholesterolemia.

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/09049

## A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07C323/20 C07C323/60 C07H15/203 A61K31/70 A61P29/00  
A61P3/06

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07C C07H A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

CHEM ABS Data, EPO-Internal, WPI Data, PAJ

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 98 51662 A (ATHEROGENICS, INC., USA) 19 November 1998 (1998-11-19)  * the whole document, in particular Table 1, pages 72-81 *  ---  -/--	1-23, 28-38, 40-42, 44-50, 52-54, 56-58, 60-62, 64-66, 68-70

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

## \* Special categories of cited documents :

\*A\* document defining the general state of the art which is not considered to be of particular relevance

\*E\* earlier document but published on or after the international filing date

\*L\* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

\*O\* document referring to an oral disclosure, use, exhibition or other means

\*P\* document published prior to the international filing date but later than the priority date claimed

\*T\* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

\*X\* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

\*Y\* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

\*Z\* document member of the same patent family

Date of the actual completion of the international search

23 August 2001

Date of mailing of the international search report

14.11.2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2  
NL - 2280 HV Rijswijk  
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,  
Fax: (+31-70) 340-3016

Authorized officer

Fitz, W

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 01/09049

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 418 648 A (HOECHST A.-G., FED. REP. GER.) 27 March 1991 (1991-03-27) * page 39, example 37; page 40, example 38; page 43, example 6 *	1,9,14, 28,30
Y	the whole document	1-23, 28-38, 40-42, 44-50, 52-54, 56-58, 60-62, 64-66, 68-70
Y	--- WO 98 51289 A (MEDFORD RUSSELL M ;SOMERS PATRICIA K (US); ATHEROGENICS INC (US)) 19 November 1998 (1998-11-19) cited in the application	1-23, 28-38, 40-42, 44-50, 52-54, 56-58, 60-62, 64-66, 68-70
Y	the whole document	
Y	--- US 5 512 595 A (REGNIER GILBERT ET AL) 30 April 1996 (1996-04-30)	1-23, 28-38, 40-42, 44-50, 52-54, 56-58, 60-62, 64-66, 68-70
Y	the whole document	
Y	--- DE MEGLIO, P. ET AL: "New derivatives of clofibrate and probucol. Preliminary studies on hypolipemic activity" FARMACO, ED. SCI. (1985), 40(11), 833-44, XP001015770	1-23, 28-38, 40-42, 44-50, 52-54, 56-58, 60-62, 64-66, 68-70
	the whole document	
	---	
	-/--	

# INTERNATIONAL SEARCH REPORT

In' stional Application No

PCT/US 01/09049

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	<p>WO 00 28332 A (ATHEROGENICS, INC., USA) 18 May 2000 (2000-05-18)</p> <p>* the whole document, in particular page 24, Table 1 *</p> <p>-----</p>	<p>1-23, 28-38, 40-42, 44-50, 52-54, 56-58, 60-62, 64-66, 68-70</p>

# INTERNATIONAL SEARCH REPORT

International application No.  
PCT/US 01/09049

## Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:  
  
Although claims 36-38,40-42,44-50,52-54,56-58,60-62,64-66,68-70 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:  
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

see further information PCT/ISA/210

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-23,28-38,40-42,44-50,52-54,56-58,60-62,64-66,68-70

Compounds of formula (I), claim 1; pharmaceutical compositions comprising them; their pharmaceutical uses for diseases mediated by VCAM-I.

2. Claims: partially: 24,39,43,51,55,59,63,67,71

Compounds of formula (II), claim 24, wherein X = O; their pharmaceutical uses for diseases mediated by VCAM-I.

3. Claims: partially: 24,39,43,51,55,59,63,67,71; completely: 25-27

Compounds of formula (II), claim 24, wherein X = S, SO or SO<sub>2</sub>; their pharmaceutical uses for diseases mediated by VCAM-I.

4. Claims: partially: 24,39,43,51,55,59,63,67,71

Compounds of formula (II), claim 24, wherein X = CH<sub>2</sub>; their pharmaceutical uses for diseases mediated by VCAM-I.

5. Claims: partially: 24,39,43,51,55,59,63,67,71

(V) Compounds of formula (II), claim 24, wherein X = NH; their pharmaceutical uses for diseases mediated by VCAM-I.

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 01/09049

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9851662 A	19-11-1998	AU 7485198 A	08-12-1998
		AU 7571198 A	08-12-1998
		BR 9809793 A	27-06-2000
		BR 9809819 A	18-09-2001
		CN 1263522 T	16-08-2000
		CN 1263462 T	16-08-2000
		EP 0994853 A	26-04-2000
		EP 0981343 A	01-03-2000
		HU 0004230 A	28-06-2001
		HU 0004592 A	28-06-2001
		NO 995543 A	10-01-2000
		NO 995544 A	10-01-2000
		PL 336788 A	17-07-2000
		SK 153199 A	16-05-2000
		SK 153299 A	16-05-2000
		TR 9902802 T	21-04-2000
		TR 9902803 T	21-07-2000
		US 6121319 A	19-09-2000
		US 6147250 A	14-11-2000
		WO 9851289 A	19-11-1998
EP 0418648 A	27-03-1991	DE 3929913 A	04-04-1991
		AT 116979 T	15-01-1995
		AU 629977 B	15-10-1992
		AU 6227790 A	14-03-1991
		CA 2024849 A	09-03-1991
		DE 59008238 D	23-02-1995
		DK 418648 T	12-06-1995
		ES 2067609 T	01-04-1995
		FI 963396 A	30-08-1996
		GR 3015360 T	30-06-1995
		HU 56085 A,B	29-07-1991
		IE 903262 A	13-03-1991
		IL 95599 A	14-07-1999
		JP 3053417 B	19-06-2000
		JP 3099075 A	24-04-1991
		KR 162081 B	01-12-1998
		NO 175002 B	09-05-1994
		NZ 235194 A	25-06-1992
		PT 95237 A,B	22-05-1991
		US 5294724 A	15-03-1994
		ZA 9007134 A	26-06-1991
WO 9851289 A	19-11-1998	AU 7485198 A	08-12-1998
		AU 7571198 A	08-12-1998
		BR 9809793 A	27-06-2000
		BR 9809819 A	18-09-2001
		CN 1263522 T	16-08-2000
		CN 1263462 T	16-08-2000
		EP 0994853 A	26-04-2000
		EP 0981343 A	01-03-2000
		HU 0004230 A	28-06-2001
		HU 0004592 A	28-06-2001
		NO 995543 A	10-01-2000
		NO 995544 A	10-01-2000
		PL 336788 A	17-07-2000
		SK 153199 A	16-05-2000
		SK 153299 A	16-05-2000

# INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/US 01/09049

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9851289 A		TR 9902802 T	21-04-2000
		TR 9902803 T	21-07-2000
		US 6121319 A	19-09-2000
		US 6147250 A	14-11-2000
		WO 9851662 A	19-11-1998
-----			
US 5512595 A	30-04-1996	FR 2704224 A	28-10-1994
		AT 157077 T	15-09-1997
		AU 667266 B	14-03-1996
		AU 6053394 A	27-10-1994
		CA 2121571 A	21-10-1994
		DE 69405036 D	25-09-1997
		DE 69405036 T	26-03-1998
		DK 621255 T	06-04-1998
		EP 0621255 A	26-10-1994
		ES 2105549 T	16-10-1997
		GR 3024942 T	30-01-1998
		JP 2885639 B	26-04-1999
		JP 6340580 A	13-12-1994
		NZ 260350 A	26-10-1995
		US 5627205 A	06-05-1997
		ZA 9402728 A	09-02-1995
-----			
WO 0028332 A	18-05-2000	AU 1911200 A	29-05-2000
		EP 1137948 A	04-10-2001
-----			